SECTION 3

- LABORATORY DIAGNOSTICS -

INTERPANDEMIC AND PANDEMIC ALERT PERIODS

A. Massachusetts Clinical and Hospital Laboratories:

- Work with state and local boards of health to address laboratory surge capacity issues and train personnel in management of respiratory specimens during an influenza pandemic.
- Send clearly labeled specimens from patients with suspected novel influenza to the State Laboratory Institute (SLI) after notifying the Massachusetts Department of Public Health (MDPH) Immunization Epidemiologists at 617-983-6800. Hospital labs should NOT attempt to isolate influenza viruses from patients with suspected novel influenza virus infection.
- Institute surveillance for influenza-like illnesses (ILI) among laboratory personnel.

B. MDPH State Laboratory Institute (SLI):

- Continue laboratory-based monitoring of seasonal influenza virus subtypes.
- Perform testing for novel subtypes of influenza viruses using real-time detection PCR (RTD-PCR) methods from the APHL and the CDC Influenza Branch.
- Perform reference level testing for influenza A/ H5 (Asian lineage) using real-time detection PCR (RTD-PCR) as a CDC-approved LRN laboratory.
- Institute surveillance for ILI among laboratory personnel.
- Participate in preparedness planning and exercises to support the response to an influenza pandemic.

PANDEMIC PERIOD

A. Massachusetts Clinical and Hospital Laboratories:

- Scale up to manage increased numbers of requests for influenza testing.
- Send selected specimens from possible pandemic influenza patients to the SLI.

B. MDPH State Laboratory Institute (SLI):

- Scale up to manage increased numbers of requests for influenza testing.
- Work with federal partners to provide healthcare providers and clinical laboratories with guidelines on all aspects of specimen management and diagnostic testing.
- Work with federal partners to monitor the pandemic virus and conduct special studies related to vaccine development, or other aspects of the response.

RATIONALE

The goals of diagnostic testing during a pandemic are to:

- Identify the earliest cases of pandemic influenza in Massachusetts.
- Support disease surveillance by the Sentinel Provider Network to monitor the pandemic's geographic spread and impact of interventions.
- Facilitate clinical treatment by distinguishing patients with influenza from those with other respiratory illnesses.
- Monitor circulating viruses for antiviral resistance.

Diagnostic testing for pandemic influenza virus may involve a range of laboratory assays, including rapid antigen tests, real-time detection reverse-transcription polymerase chain reaction (RTD-PCR), virus isolation, and immunofluorescence antibody (IFA) assays. During the earliest stages of a pandemic, public health, hospital, and clinical laboratories might receive a large and potentially overwhelming volume of clinical specimens. Pre-pandemic planning is therefore essential to ensure the timeliness of diagnostic testing and the availability of diagnostic supplies and reagents, address staffing issues, and disseminate protocols for safe handling and shipping of specimens. Once a pandemic is underway, the need for laboratory confirmation of clinical diagnoses may decrease as the virus becomes widespread.

http://www.hhs.gov/pandemicflu/plan/ - skip

OVERVIEW

This section of the overall Massachusetts Influenza Preparedness Plan focuses on laboratory guidelines for the use of diagnostic tests to detect, characterize, and monitor novel subtypes of influenza, including avian influenza A (H5N1) and other viruses with pandemic potential. Specifically, the Interpandemic and Pandemic Alert Period sections focus on laboratory testing in support of seasonal influenza surveillance, laboratory-based detection of novel influenza subtypes, and preparedness planning to support the laboratory component of the response to a pandemic (e.g., detection and characterization of viruses, case reporting, specimen management, surge capacity). The Pandemic Period section focuses on the provision of laboratory support for disease surveillance to assist clinicians and hospitals. The plan also covers occupational health issues for laboratory workers.

http://www.hhs.gov/pandemicflu/plan/ - skip

INTERPANDEMIC AND PANDEMIC ALERT PERIODS

A. Laboratory support for seasonal influenza surveillance

MDPH's Sentinel Provider Program submits data for Massachusetts as a member of the World Health Organization (WHO) Global Influenza Surveillance Network and the National Respiratory and Enteric Virus Surveillance System (NREVSS) that provides laboratory-based surveillance for new subtypes of influenza throughout the United States. Currently, 39 sites are enrolled throughout Massachusetts.

B. Laboratory testing for novel influenza subtypes

MDPH, along with local boards of health, hospitals, and clinicians are performing enhanced surveillance to identify patients who may present with possible cases of novel influenza based on CDC defined clinical criteria (see below). As new updates to the guidance occur or urgent situations arise, MDPH will continue to utilize the Health and Homeland Alert Network (HHAN) to keep local boards of health, hospitals, and clinicians informed.

As part of this surveillance, the CDC is urging providers to carry out enhanced surveillance in travelers with severe unexplained respiratory illness returning from H5N1-affected countries.

a. Patients who *should* be evaluated for avian influenza:

Testing for avian influenza A (H5N1) http://www.cdc.gov/flu/avian/outbreaks/ -h5n1is indicated for hospitalized patients who fit the following high-risk criteria:

- Radiographically confirmed pneumonia, acute respiratory distress syndrome (ARDS), or other severe respiratory illness for which an alternate diagnosis has not been established.

AND

- History of travel, within 10 days of symptom onset, to a country with documented H5N1 avian influenza in poultry and/or humans (for a regularly updated listing of H5N1-affected countries, see the World Organization of Animal Health (OIE) website at http://www.oie.int/eng/en_index.htm and the WHO website at http://www.who.int/en/.

For patients whom fit these criteria, notify the Massachusetts Department of Public Health (MDPH) at (617) 983-6800 (24/7) immediately and ask to speak to the On-call Immunization Epidemiologist whom will arrange for collection and transport of specimens for diagnostic testing.

b. Patients who should be *considered* for avian influenza testing:

Testing for avian influenza A (H5N1) should be considered on a case-by-case basis in consultation with MDPH epidemiologists for hospitalized or ambulatory patients with:

- Documented temperature of >38°C (>100.4°F); AND
- One or more of the following: cough, sore throat, shortness of breath; AND
- History of contact with poultry (e.g., visited a poultry farm, a household raising poultry, or a bird market) or with a known or suspected human case of influenza A (H5N1) in an H5N1-affected country within 10 days of symptom onset.

C. Laboratory planning to support the response to an influenza pandemic

Advance planning is essential to anticipate adequate laboratory capacity to support medical and public health partners during an influenza pandemic. MDPH is coordinating surge capacity planning utilizing existing bioterrorism preparedness plans.

a. Detection and characterization of novel influenza strains

The State Laboratory Institute is proficient to perform RTD-PCR for molecular detection of Influenza types A and B and subtypes H1, H3, H5, and H7. A positive RTD-PCR test result for a novel influenza strain should be considered presumptive, pending testing by a second reference laboratory.

SLI will send specimens to CDC for confirmation if:

- A sample is positive for H5 or another novel subtype by RTD-PCR.
- ii. A sample from a patient who meets the clinical and epidemiologic criteria for possible infection with a potentially pandemic virus is positive for influenza A and negative for H1, H3, H5, or H7 subtypes by RTD-PCR.

Detailed information on how to contact the SLI when a novel influenza subtype is suspected and how to handle, label, and ship clinical specimens for diagnostic testing is provided on the MDPH website (www.mass.gov/dph).

b. Laboratory reporting

MDPH's Sentinel Provider Network reports laboratory-confirmed seasonal influenza cases to CDC utilizing the Public Health Information System (PHLIS), and a web-based NREVSS data-entry system. Cases of novel influenza will be reported to CDC by the same mechanisms.

MDPH has requested funding to improve its Laboratory Information Management System (LIMS) to handle increases in specimen submissions, data management of the laboratory test information and reporting. This system will also be integrated with MDPH's Surveillance Programs.

c. Distribution of diagnostics reagents and test information

The State Laboratory Institute is approved by the CDC's Laboratory Response Network (LRN) to perform reference level testing for influenza A/H5 (Asian lineage) real-time detection PCR. Additionally, SLI has implemented APHL/CDC assays for performing Influenza molecular typing A and B and subtyping of H1, H3, H5, and H7. SLI will continue to update its testing capabilities based on guidance from the CDC regarding diagnostic tests and reagents available via the LRN and HHAN.

d. Laboratory surge capacity planning

The State Laboratory Institute is assessing needs for scaled-up diagnostic testing activity during the early stages of a pandemic as they relate to: laboratory staffing, training, reporting, equipment and supplies. MDPH is developing strategies to address these needs including:

i. Staffing and training

- Cross-training personnel during the regular influenza season in the use of rapid diagnostic tests and RTD-PCR protocols
- Training additional SLI staff to perform data entry
- Training additional SLI staff to prepare Virus Isolation kits
- Updating surge protocols for laboratory testing staff to utilize rotating shifts

ii. Supplies and equipment

- SLI is developing strategies for acquiring adequate diagnostic supplies and equipment to process large numbers of samples during the initial stages of a pandemic by:
    - Establishing the current level of diagnostic supplies, including personal protective equipment for laboratorians (e.g., gloves, masks).
    - Assessing anticipated equipment and supply needs, and determining a trigger point for ordering extra resources. Considerations for back-up sources of supplies and equipment will be assessed.
- Determining how consumption of supplies will be tracked during a pandemic.
- Purchasing equipment that can meet the needs of increased testing requirements.

iii. Specimen management

- MDPH has requested funding to improve its Laboratory Information Management System (LIMS) to handle increases in specimen submissions, data management of the laboratory test information and reporting. This system will also be integrated with

MDPH's Surveillance Programs.

iv. Specimen packaging and shipping

- Guidelines for Collecting and Shipping Specimens for Influenza Diagnostics have been prepared and include information on safety issues related to specimen handling. See MDPH website (insert website) for details.
- Although procedures for specimen collection, handling, and shipping during a pandemic will be the same as those used for seasonal disease surveillance, laboratory staff is discussing strategies for receiving and processing larger numbers of specimens in a very short time, especially during the early stages of a pandemic. It is understood that once the pandemic is underway and healthcare providers rely on clinical criteria and rapid test kits, more diagnostic activities may be conducted locally and fewer viral isolation kits will need to be shipped from MDPH with the exception of those required for surveillance purposes.

v. Partnerships with healthcare providers and clinical laboratories

Good working relationships between healthcare providers and public health laboratories will facilitate diagnostic activities during a pandemic.

- MDPH is continuing to build partnerships with healthcare providers in their jurisdictions, including physicians who participate in the Sentinel Provider Network (SPN) during the regular influenza season.
- MDPH is collecting contact information and testing capability from clinical laboratorians as a means of assessing capacity.

http://www.hhs.gov/pandemicflu/plan/ - skip**PANDEMIC PERIOD**

A. Laboratory support for disease surveillance

- Public health, hospital, and clinical laboratories will support surveillance for pandemic influenza through the same mechanisms that support laboratory-based surveillance for seasonal influenza. SLI will continue to work with the CDC and the LRN to provide diagnostic testing for the pandemic virus using molecular methods (RTD-PCR).
- The SLI will update its testing capabilities as soon as a pandemic strain has been identified and the CDC's Influenza Laboratory has developed and disseminated additional or new reagents.
- As the pandemic unfolds, MDPH will communicate CDC advisories on when confirmatory testing (i.e., sub-typing) is required in Massachusetts. Although confirmatory testing will be required when the pandemic begins, the level of testing will decrease as the virus becomes widespread.
- MDPH will coordinate ongoing CDC advisories on the percentage of isolates per week or month that should send to CDC from Massachusetts as part of efforts to monitor changes in the antigenicity and antiviral susceptibility of the pandemic virus.
- The MDPH's Sentinel Provider Network may be asked to assist the U.S.-based WHO collaborating laboratories, NREVSS laboratories, and/or Emerging Infectious Program sites (www.cdc.gov/ncidod/osr/site/eip/index.htm) in conducting special studies or establishing additional laboratory-based surveillance systems to answer critical questions related to vaccine development or other aspects of the public health response. Specifically, MDPH may be asked, for example, by CDC to coordinate serosurveys to determine the number of persons who develop antibodies to the pandemic virus over time.

B. Laboratory support for clinicians

When a pandemic begins, clinical laboratories will scale up to manage increased numbers of requests for influenza testing. As part of this effort, MDPH will continue to implement updated CDC guidelines for safe handling, processing, and rapid diagnostic testing of clinical specimens from patients who meet the case definition for pandemic influenza and provide this information on the MDPH website (www.mass.gov/dph).

If private laboratories perform PCR testing during the early phase of an influenza pandemic, the results must be confirmed by the SLI and testing information must be provided to the MDPH Immunization Program.

MDPH has made available to local healthcare providers:

- A detailed guidance document titled, "Interim Guidance for Clinicians and Laboratorians Regarding Avian Influenza A (H5N1)" that includes screening criteria; specimen collection and submission; testing; treatment information, etc. website (www.mass.gov/dph) Information regarding rapid communication of test results and reminders that a negative test result (especially by rapid diagnostic testing) might not rule out influenza and should not affect patient management or infection control decisions.
- Guidance on the use of commercially available rapid diagnostic tests for the detection of influenza A. These tests may be used by physicians to supplement clinical diagnoses of pandemic influenza. Because the sensitivity of rapid diagnostic kits might not be optimal, physicians should take their positive and negative predictive values into consideration when interpreting test results.

C. Bio-containment procedures

During an influenza pandemic, laboratory procedures should be conducted under appropriate bio-safety conditions:

- Commercial antigen detection testing for influenza should be conducted using BSL-2 work practices.
- The State Laboratory Institute will conduct specimen preparation using BSL-3 practices and complete RTD-PCR testing using BSL-2 work practices.

D. Occupational health issues for laboratory workers

To protect the health of laboratory workers during a pandemic, MDPH's SLI will maintain the following safety practices during the interpandemic and pandemic alert periods:

- Conduct laboratory procedures under appropriate bio-containment conditions.
- Encourage routine vaccination of all eligible laboratory personnel who are exposed to specimens from patients with respiratory infections.
- Implement a medical surveillance program for laboratory personnel based on federal guidelines.